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(54) **New polysaccharide esters.**

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Description

The present invention concerns total esters of acidic polysaccharides chosen from the group formed by carboxymethylcellulose, carboxymethyl starch and carboxymethylchitin wherein the carboxy groups of said polysaccharide are esterfied with an alcohol of the aliphatic, araliphatic, cycloaliphatic and heterocyclic series, whereby the alcohols of the aliphatic series have a maximum of 34 carbon atoms and are unsubstituted or substituted by one or two functional groups chosen from the group formed by amino, hydroxy, mercapto, aldehydo, keto, carboxy, hydrocarbyl and dihydrocarbylamino, ether, ester, thioether, thioester, acetal, ketal, carbalkoxy groups, carbamidic and substituted carbamidic groups by one or two alkyl groups with the hydrocarbyl radicals in these functionally modified groups having a maximum of 6 carbon atoms, and in which such alcohols of the aliphatic series may be interrupted in the carbon atom chain by heteroatoms chosen from the group formed by oxygen, sulfur and nitrogen,

the alcohols of the araliphatic series are those with only one benzene residue and in which the aliphatic chain has a maximum of 4 carbon atoms and in which the benzene residue may be substituted by between 1 and 3 methyl or hydroxy groups, by halogen atoms, and in which the aliphatic chain may be substituted by one or two functions chosen from the group formed by free amino or mono- or diethyl groups or by pyrrolidine or piperidine groups, and

the alcohols of the cycloaliphatic or aliphatic-cycloaliphatic or heterocyclic series respectively derive from mono- or polycyclic hydrocarbons with a maximum of 34 carbon atoms and are unsubstituted or substituted by one or more functional groups chosen from the group formed by amino, hydroxy, mercapto, aldehydo, keto, carboxy, hydrocarbyl and dihydrocarbylamino, ether, ester, thioether, thioester, acetal, ketal, carbalkoxy, carbamidic and substituted carbamidic groups by one or two alkyl groups with the hydrocarbyl radicals in these functionally modified groups having a maximum of 6 carbon atoms, and which may be interrupted in the carbon atom chain by heteroatoms chosen from the group forced by - O -,

- S -, and which may have one or more bonds, including aromatic structures.

The invention also includes the use of these new esters as medicaments, for the manufacture of pharmaceutical and cosmetic preparations, in the sector of biodegradable plastic materials and, therefore, for the manufacture of medical, surgical and sanitary articles, in galenicals and in numerous industrial sectors in the place of acidic polysaccharides now in use, such as alginic acid, especially in the food industry. The invention also includes the articles resulting from these various uses.

The carboxymethyl derivatives of the abovesaid natural polysaccharides, can be obtained by methods described in literature, essentially by treatment of the sane with haloacetic acids, such as chloracetic acid, or their salts. The polysaccharides used in these preparation methods and which are therefore the basis of the new esters of the present invention, may have a wide range of molecular weights, such as those of the various types of starch, of cellulose and chitin present in natural materials.

There are already reports in literature of "carboxymethylcellulose esters" prepared by alkylation of the carboxy hydroxyl with diazomethane or with the alcohol corresponding to the alkyl groups to be introduced in the presence of a strong acid. In this way partial esters are obtained which do not however seem to be pure esters. Thus, in the German patent No. 957,938 carboxymethylcellulose is esterified at about 0 °C with alcohol (methyl, propyl, butyl and octyl) and gasseous hydrochloric acid. In the case of methyl alcohol the reaction is effected over a period of 48 hrs, long enough for the glucoside structures present in the polysaccharide to be destroyed and no longer remain intact (see: Methanolysis of Polysaccharides; Carbohydrate Research 168 (1987) 103-109).

The same can be said of the products obtained according to the procedure described in U.S. patent No. 2,912,430. The preparation procedure for the methyl ester of carboxymethylcellulose described in LATV; PSR Zinat. Akad. Vestis. Kim. r. 1982/5 624-7 regards carboxymethylcellulose with diazomethane; this reagent is too drastic to leave intact the alcoholic hydroxyl groups of the polysaccharide; this ester is to be considered an ether ester of carboxymethylcellulose.

Other preparations have been made of esters of bivalent alcohols of carboxymethylcellulose obtained by the action on the same of ethylene or propylene oxides (see Belgian patent No. 656,949, Japanese patents No.s 70.36.143 and 74.18.981). Unknown however are esters of superior bivalent alcohols, that is, those with 4 or more carbon atoms.

Some esters of monovalent alcohols of carboxymethyl starch have been described too: thus, in the publication "Staerke" 1977, 29(4), 126-8, two types of carboxymethyl starch, one with low viscos-

ity and one with high viscosity were benzylated with benzyl chloride in alkaline conditions at 60° and benzyl esters were obtained, in which however the polysaccharide was found to be partially decarboxymethylated.

The methyl ester of carboxymethyl starch was prepared by reacting starch with methylmonochloroacetate in methanol or benzene solution. The product proved to be esterifed to an extent of about 50% (Zesz. Nauk. Politech. Lodz, Che. Spozyw. 1977, 29, 5-17).

No carboxymethylchitin esters have been described in literature.

EP-A 0 104 467 describes carboxymethylcellulose esters obtained by esterfication with alcohols in the presence of acids.

US-A 3 092 619 discloses carboxymethylcellulose and carboxymethystarch esters which are obtained by reaction with epoxides.

EP-A 0 251 905 describes the preparation of total and partial esters of alginic acid.

The esters of the carboxymethyl derivatives of the abovesaid polysaccharides obtained according to the abovesaid methods are always partial esters. Up till now it has not been possible to prepare total esters by such methods. Thanks to a new procedure of the present invention, it is now possible to have access to the total esters of the abovesaid carboxymethyl derivatives too. The new method consists in treating quaternary ammonium salts of the abovesaid acidic polysaccharides with an alkylating or etherifying agent in an aprotic solvent, especially in dimethylsulfoxide. By this method it is possible to prepare not only the total esters of the abovesaid monovalent or bivalent alcohols, but also the whole range of esters deriving too from alcohols of other series, such as alicyclic or heterocyclic esters, even those with quite complicated structures, which could not be obtainable by the prior methods used in the art.

As a result, one of the main objects of the present invention is to provide new total esters of the polysaccharides chosen from the group formed by carboxymethylcellulose, carboxymethyl starch and carboxymethylchitin with alcohols of the aliphatic, araliphatic, cycloaliphatic or heterocyclic series. A second object of the invention is represented by a new procedure for the preparation of esters of carboxymethylcellulose, carboxymethyl starch and carboxymethylchitin, characterized by treating a quaternary ammonium salt of one of these polysaccharide derivatives with an etherifying agent in an aprotic solvent.

A third object of the invention is represented by the use of esters of the abovesaid derivatives of the three carboxymethylpolysaccharides, including the known ones, in the fields of medicine, pharmaceuticals and cosmetics and in the following industrial sectors:

1. food industry
2. paper industry
3. adhesive products
4. printing
5. textile dyes
6. in the preparation of sanitary, medical and surgical products
7. in galenics for the preparation of capsules and microcapsules
8. in biology to immobilize enzymes
9. as emulsifyers for polishes, anti-foam agents, lactics and as stabilizers in the ceramic and detergent industries

A fourth object of the invention is represented by industrial articles or products made with esters for the aforesaid uses and which will be described in more detail hereafter.

The esters of the present invention may themselves be medicaments, whenever the alcohols which make up the ester group are therapeutically active. In such cases the polysaccharide ester acts as a vehicle for such therapeutically active substances and medicaments in the form of such esters, possibly associated with other conventional excipients for pharmaceutical preparations. These esters have properties which are qualitatively similar to those of the therapeutically active alcohol used as the esterifying agent. However, the new esters of the invention have a more differentiated range of action, even with regard to the known esters, ensuring a more balanced, constant and regular pharmacological action and usually achieving a marked retard effect.

One particular case of such medicaments is represented by esters in which one part of the carboxy groups is esterified with therapeutically active alcohols and another part with pharmacologically indifferent alcohols, or whose activity is negligible. By suitably dosing the percentages of the two types of alcohol as esterifying component, it is possible to obtain esters with the same activity as the pharmacologically active alcohol and in which the abovesaid properties of increased bioavailability and stability are made full use of. Lastly, it is possible to prepare mixed-type esters in which the ester groups derive from two different therapeutically active alcohols, for example from a cortisone steroid and from an antibiotic.

It is however also possible to prepare esters with three or more alcohol components, for example esters in which part of the carboxy groups are esterifed with a therapeutically active alcohol, another part with another therapeutically active alcohol and a third part with a therapeutically inactive alcohol.

The vehicling of therapeutically active substances, apart from the esterification of

therapeutically active alcohols, can also be achieved by the simple association of an ester of the type of the present invention (new or known) with the therapeutically active substance, that is, in a physical mixture. In this case it is preferable to use carboxymethyl esters derived from cellulose, starch and chitin esters with therapeutically indifferent alcohols, and the therapeutically active substance may be for example of an acidic or neutral character. Regarding the vehicling action of the new esters it is possible therefore to prepare new medicaments including:

1. a pharmacologically active substance or an association of two or more such substances; and
2. a total ester of a carboxymethyl derivative of cellulose, starch, or chitin and such medicaments are a further object of the invention.

The esters to be used in these medicaments are above all those in which the esterifying alcohol is itself not pharmacologically active, for example a simple aliphatic alcohol, such as one of those named hereafter. The invention does not however exclude medicaments of this type in which the ester too is pharmacologically active, such being the case for example of one of the abovesaid esters deriving from pharmacologically active alcohols.

Carboxymethyl-polysaccharide esters are particularly useful as vehicles in ophthalmology, where a particular compatibility is to be noted between the new products and the corneal epithelium, and therefore excellent tolerability with no sensitization effects.

Furthermore, when the medicaments are administered in the form of concentrated solutions with elastic, viscous characteristics or in solid form, it is possible to obtain homogenous, stable, perfectly transparent and adhesive films on the corneal epithelium which also guarantee prolonged bioavailability of the drug and which represent excellent retard effect preparations. Such ophthalmic medicaments are exceptionally valuable in the veterinary field, considering that there are at present no veterinary preparations containing chemotherapeutic substances for use in the eyes. Indeed, preparations for human use are normally used for animals too, and these do not always guarantee a specific range of action or they do not always allow for the particular conditions under which treatment must take place. This is the case, for example of therapy for infectious keratoconjunctivitis, pink eye or IBK, an infection which mainly affects cattle, sheep and goats. Presumably these three species have specific etiologic factors and more particularly: in cattle the main microorganism involved would appear to be Moraxella bovis (even though it is not possible to exclude other agents of a viral origin, such as Rhinotracheitis virus, in sheep Micoplasma, Rickettsiae and Clamidiae, in goats Rickettsiae).

The disease manifests itself in acute form and tends to spread rapidly: in the initial stages the symptoms are characterized by blepharospasm and excessive lacrimation, followed by purulent exudate, conjunctivitis and keratitis, often associated with high temperature, reduced appetite and milk production. Particularly serious are the corneal lesions which in the final stages may even cause perforation of the cornea itself. The clinical course of the disease varies from a few days to several weeks. A vast range of chemotherapeutic agents are used in treatment, administered both topically (often associated with steroid antiinflammatory agents), and systemically, and among these are: tetracyclines, such as oxytetracycline, penicillins, such as cloxacillin and benzylpenicillin, sulfamides, polymixin B (associated with miconazole and prednisolone), chloramphenicol and tylosin. Topical treatment of the disease, despite its apparent simplicity, is still open to debate, since the ocular preparations used to date do not, for one reason or another, allow therapeutically efficacious concentrations of antibiotic or sulfamide to be obtained in the tears. This is understandable in the case of solutions, considering the predominantly tilted position of the head in the above animals, but it is also true of the semisolid medicaments, as the excipients normally used in the same do not adhere sufficiently to the surface of the cornea, since they do not generally have a high enough concentration of active substance and are impossible to satisfactorily distribute over the surface to be treated (presence of a distribution gradient).

These drawbacks to conventional eye drops used in ophthalmology have been described by Slatter et al. in "Austr. vet. J.," 1982, 59 (3), pp. 69-72.

With the esters of the present invention these difficulties can be overcome. The presence of carboxymethyl-polysaccharide ester as vehicle for ophthalmic drugs does indeed allow the formulation of excellent preparations free from concentration gradients of the active substance and therefore perfectly homogenous, perfectly transparent and perfectly adhesive to the corneal epithelium, free from sensitization effects and with the active substance contained in an excellent vehicle and possibly with a retard effect.

The above properties of the new medicaments can of course also be put to use in other fields besides ophthalmology: they can be applied in dermatology and in infections of the mucus, for example of the mouth.

They can also be used to obtain a systemic effect thanks to transcutaneous absorption, for example in suppositories. All these applications are

feasible both in human and veterinary medicine. In human medicine the new medicaments are particularly suitable for use in paediatrics. The present invention therefore also includes in particular any one of these therapeutic applications.

For the sake of brevity, reference hereinafter to the active substance of component 1) according to the invention should be understood to encompass the presence of a single active substance and also the association or mixture of two or more active substances.

Component 1) defined above may first and foremost be enumerated according to its use in various fields of therapy, beginning with the distinction between human and veterinary medicine and then specifying the various sectors of application with regards to the organs or tissues to be treated, such as ophthalmology, dermatology, otorhinolaryngology, gynaecology, angiology, neurology or any other type of pathology of the internal organs which can be treated by topical applications, such as rectal applications. According to one particular aspect of the present invention, the pharmacologically active substance 1) is first and foremost a substance for ophthalmic use. On the basis of another criterion the pharmacologically active substance 1) should be distinguished with regard to its effect and may therefore, for example, be in the form of an anesthetic, analgesic, antiinflammatory drug, a vasoconstrictor, antibacterial, or antiviral. For the ophthalmic sector it can be indicated particularly and for example for its: miotic, antiinflammatory, wound healing and antimicrobial effects. Component 1) may also be, according to the invention, an association of two or more active substances, as contained in many known medicaments. For example, in ophthalmology, they may be associated with an antibiotic, an antiphlogistic and a vasoconstrictor or with several antibiotics one or more antiphlogistics, or with one or more antibiotics, a mydiatric or miotic or wound healing agent or an antiallergic etc. For example the following associations of ophthalmic drugs may be used: kanamycin + phenylephrine + dexamethasone phosphate, kanamycin + betamethasone phosphate + phenylephrine, or similar associations with other antibiotics used in ophthalmology, such as rolitetracycline, neomycin, gentamycin, tetracycline. In dermatology it is possible to have as active component 1) associations of various antibiotics, such as erythromycin, gentamycin, neomycin, gramicidin, polymyxin B, between themselves, or of the same antibiotics with antiinflammatory agents, for example corticosteroids, for example hydrocortisone + neomycin, hydrocortisone + neomycin + polymyxin B + gramicidin, dexamethasone + neomycin, fluorometholone + neomycin, prednisolone + neomycin, triamcinolone + neomycin + gramicidin + nystatin, or any other association used in conventional dermatological preparations. Associations of different active substances are not of course limited to this field, but in each of the abovesaid fields of medicine it is possible to use associations similar to those already in use for the pharmaceutical preparations known to the art.

According to one preferential aspect of the invention however, medicaments containing the carboxymethylpolysaccharide ester are used alone as the vehicle with therapeutically active or inactive substances (apart from possibly aqueous solvent). Also included in the invention are those mixtures obtainable for all the types of medicament described here and also mixtures of such medicaments.

Examples of pharmacologically active substances 1) to be used in ophthalmic medicaments according to the invention are: basic or nonbasic antibiotics, for example aminoglycosides, macrolides, tetracyclines and peptides, for example gentamycin, neomycin, streptomycin, dihydrostreptomycin, kanamycin, amikacin, tobramycin, spectinomycin, erythromycin, oleandomycin, carbomycin, spiramycin, oxytetracycline, rolitetracycline, bacitracin, polymyxin B, gramicidin, colistin, chloramphenicol, lincomycin, vancomycin, novobiocin, ristocetin, clindamycin, amphotericin B, griseofulvin, nystatin and possibly their salts, such as sulfates or nitrates, or associations between themselves or with other active principles, for example those named hereafter.

Other ophthalmic drugs to be used to advantage according to the present invention are: other antiinfectious agents such as diethylcarbamazine, mebendazole, sulfamidics such as sulfacetamide, sulfadiazine, sulfisoxazole; antivirals and antitumorals such as iododeoxyuridine, adenine arabinoside, trifluorothymidine, acyclovir, ethyldeoxyuridine, bromovinyldeoxyuridine, 5-iodo-5′-amino-2′,5′-dideoxyuridine; steroid antiinflammatories, for example dexamethasone, hydrocortisone, prednisolone, fluorometholone, medrisone and possibly their esters, for example phosphoric acid esters; nonsteroid antiinflammatory agents, for example indomethacin, oxyphenbutazone, flurbiprofen; wound healers such as the epidermal growth factor EGF; local anesthetics, such as Benoxinate, proparacain and possibly their salts; cholinergic agonist drugs such as pilocarpine, methacholine, carbamylcholine, aceclidine, physostigmine, neostigmine, demecarium and possibly their salts; cholinergic antagonist drugs such as atropine and its salts; adrenergic agonist drugs such as noradrenalin, adrenalin, naphazoline, methoxamine and possibly their salts; adrenergic blockers such as propanolol, timolol, pindolol, bupranolol, atenolol, metoprolol,

oxprenolol, practolol, butoxamine, sotalol, butedrin, labetalol and possibly their salts.

Also, associations of such drugs between themselves and possibly with other principles may be used as component 1) according to the invention.

Examples of active substances to be used alone or in associations between themselves or with other active principles in dermatology are: therapeutic agents such as anti-infectious agents, antibiotics, antimicrobials, antiinflammatories, cytostatics, cytotoxics, antivirals, anesthetics, and preventive agents, such as sun shields, deodorants, antiseptics and disinfectants. Among the antibiotics are erythromycin, bacitracin, gentamycin, neomycin, aureomycin, gramicidin and associations of the same, the anitbacterials and disinfectants include nitrofurazone, mafenide, clorexidine, and derivatives of 8-hydroxychinoleine and possibly their salts; the antiinflammatories include above all corticosteroids such as prednisolone, dexamethasone, flumethasone, clobetasol, acetonide of triamcinolone, betamethasone or their esters, as valerianates, benzoates, dipropionates; as cytotoxics fluorouracil, methotrexate, podophyllin; among the anesthetics are dibucaine, lidocaine, benzocaine.

The items in this list are of course only examples and any other agent described in literature may be used.

From the examples given for ophthalmology and dermatology it is possible to deduce which medicaments according to the present invention are to be used in the above fields of medicine, for example in otorhinolaryngology or odontology or in internal medicine, for example in endocrinology, where it is possible to use preparations for intradermal absorption or through the mucus, for example rectal or intranasal absorption, for example as nasal sprays or for inhalation into the oral cavity or into the pharynx.

Such preparations may therefore be for example antiinflammatories, or vasoconstrictors or vasopressors such as those named for ophthalmology, vitamines, antibiotics, such as those named above, hormones, chemotherapeutic agents, antibacterials, etc. also as named above for use in dermatology.

The medicaments according to the invention may be in solid form, for example as freeze-dried powders containing only the two components mixed together or prepared separately.

Such medicaments in solid form, on contact with the epithelium to be treated, create more or less concentrated solutions according to the nature of the particular epithelium, with the same characterisitics as the solutions previously prepared in vitro and which represent another particularly important aspect of the present invention. Such solutions are preferably in distilled water or in sterile physiological solutions and contain preferably no other pharmaceutical vehicle other than carboxymethylpolysaccharide ester. Concentrations of such solutions may also vary within a wide range, for example between 0.01 and 75% both for each of the two separate components and for their mixtures or salts. Particular preference is given to solutions with a marked elastic, viscous character, for example with a content of between 10% and 90% of the medicament or of each of its two components.

Particularly important are medicaments of this type, both in an anhydrous form (freeze-dried powders) or as solutions, either concentrated or diluted in water or saline, possibly with the addition of additive or auxiliary substances, such as in particular disinfectant substances or mineral salts acting as buffer or others, for ophthalmic use.

Among the medicaments of the invention the ones to be chosen in each case, are the ones with a degree of acidity suitable for the environment to which they are to be applied, that is, with a physiologically tolerable pH.

The pharmaceutical preparations containing therapeutically active carboxymethylpolysaccharide esters, possibly in the form of the abovesaid medicaments resulting from the association of components 1) and 2), contain common excipients and may be used for oral, rectal, parenteral, subcutaneous, local or intradermal use. They are therefore in solid or semisolid form, for example pills, tablets, gelatinous capsules, capsules, suppositories, soft gelatin capsules. For parenteral and subcutaneous use it is possible to use forms intended for intramuscular or intradermal use, or suitable for infusions or intravenous injections and can therefore be presented as solutions of the active compounds or as freeze-dried powders of the active compounds to be mixed with one or more pharmaceutically acceptable excipients or diluents, suitable for the abovesaid uses and whose osmolarity is compatible with the physiological fluids. For local use, preparations in the form of sprays come into consideration, for example nasal sprays, creams or ointments for topical use or sticking plasters specially prepared for intradermal administration.

The preparations of the invention may be used for administration to man or animals. They contain preferably between 0.01% and 10% of active component per solutions, sprays, ointments and creams and between 1% and 100% and preferably between 5% and 50% of active compound for the preparations in solid form. The dosage to be administered depends on specific indications, on the desired effect and on the chosen administration route. Daily doses of such preparations can be

deduced by considering that used for the corresponding known preparations for corresponding cures of the therapeutically active alcohol whose action is to be exploited. Thus, for example, dosage of a carboxymethylchitin ester with cortisone can be derived from its content of this steroid and from its usual dosage in the known pharmaceutical preparations.

One particular form of pharmaceutical preparations is represented by the abovesaid medicaments constituted bv the association of a carboxymethylpolysaccharide ester by an active substance, for example for topical use. These may also be in solid form, for example as freeze-dried powders containing only the two components 1) and 2) in a mixture or packed separately. Such medicaments in solid form, on contact with the epithelium to be treated, create more or less concentrated solutions according to the nature of the particular epithelium with the same characteristics as the solutions previously prepared in vitro and which represent another particularly important aspect of the present invention. Such solutions are preferably in distilled water or in sterile physiological solutions and contain preferably no other pharmaceutical vehicle other than the ester of carboxymethylpolysaccharide or one of its salts. Concentrations of such solutions may also vary within a wide range, for example between 0.01 and 75% both for each of the two separate components and for their mixtures or salts. Particular preference is give to solutions with a marked elastic, viscous character, for example with a content of between 10% and 90% of the medicament or of each of its two components.

Particularly important are medicaments of this type, both in an anhydrous form (freeze-dried powders) or as concentrated solutions or diluted in water or saline, possibly with the addition of additive or auxiliary substances, such as in particular disinfectant substances or mineral salts acting as buffer or others, for ophthalmic use.

Among the medicaments of the invention, the ones to be chosen in each case, are the ones with a degree of acidity suitable for the environment to which they are to be applied, that is, with a physiologically tolerable pH.

In the cosmetic articles according to the invention, the esters of carboxymethylpolysaccharides are mixed with excipients commonly used in the art and are for example those already listed above for pharmaceutical preparations. Above all are used creams, ointments, lotions for topical use in which the carboxymethylpolysaccharide ester may constitute the cosmetic active principle possibly with the addition of other cosmetically active principles, such as for example steroids, for example pregnenolone, or one of the principles reported above. In such preparations the polysaccharide ester may be an ester with a cosmetically active alcohol, such as dexpantenol, or also an ester with a cosmetically inactive alcohol, such as inferior aliphatic alcohol, for example one of those named. The effect is due to the intrinsic cosmetic properties of the polysaccharide component. The cosmetic articles can however be based on various other active principles, for example disinfectant substances or sunshields or waterproofing agents or regenerating or antiwrinkle substances, or odoriferous substances, especially perfumes. In this case the polysaccharide ester may itself be the active ingredient and derive from alcohols which have such properties, for example from superior aliphatic alcohols or terpene alcohols in the case of perfumes or may function above all as a vehicle for substances with such properties as are associated with them. Particularly important are therefore cosmetic compositions similar to the medicaments described above in which the pharmaceutically active component 1) is substituted by a cosmetological factor, and the respective salts. Use of the abovesaid esters deriving from alcohols used in the perfume industry represents a big step forward in technique, since it allows for slow, constant and prolonged release of the odorous principles.

An important application of the present invention concerns sanitary and surgical articles, the methods for their manufacture and their use. The invention therefore embraces all articles similar to those already on the market but containing an ester of carboxymethyl-cellulose, -starch or -chitin, for example inserts or ophthalmic lenses.

Absolutely new surgical and sanitary articles according to the present invention are represented by esters of carboxymethyl-polysaccharide acid regenerated as such by appropriate organic solutions, suitable to be made into sheet or thread form, obtaining films, sheets and threads for use in surgery, as auxiliaries and skin substitutes in severe cases of damage to this organ, such as for example following burns, or as suture threads in surgical operations. The invention includes in particular these uses and a procedure for the preparation of such articles consisting of (a) forming a solution of polysaccharide ester in a suitable organic solvent, for example a keton, an ester or an aprotic solvent such as an amide of a carboxy acid, especially a dialkylamide or of an aliphatic acid with between 1 and 5 carbon atoms and deriving from alkyl groups with between 1 and 6 carbon atoms, and especially from an organic sulfoxide, that is a dialkylsulfoxide with alkyl groups with a maximum of 6 carbon atoms, such as especially dimethylsulfoxide or diethylsulfoxide and also especially a fluorurate solvent with a low boilong point, such as especially hexafluoro-isopropanol, (b) working this solution into sheet or thread form

and (c) removing the organic solvent by contact with another organic or aqueous solvent which will mix with the first solvent and in which the polysaccharide ester is insoluble, especially an inferior aliphatic alcohol, for example ethyl alcohol (Wet spinning), or, should a solvent with a not too high boiling point be used to prepare the solution of the polysaccharide derivative, (d) removing this solvent in dry conditions with a current of gas, especially suitably heated nitrogen (Dry spinning). Dry-wet spinning can also be used to great effect.

The threads obtained with the esters of carboxymethyl-polysaccharide acids may be used to prepare lints for use in the medication of injuries and in surgery. These lints have the extraordinary advantage of being biodegradable in the organism, thanks to the enzymes they contain. Such enzymes split the ester into carboxymethyl-polysaccharide acid and the corresponding alcohol, should an ester deriving from a therapeutically acceptable alcohol be used, such as ethyl alcohol.

Preparation of the abovesaid sanitary and surgical articles can include the addition of plastifying materials to improve their mechanical characteristics, such as in the case of threads, to improve their resistance to tangles. These plastifying materials may be for example alkaline salts of fatty acids, for example stearate of sodium or palmitate of sodium, the esters of organic acids with a high number of carbon atoms, etc. Another application of the new esters where their biodegradability is taken advantage of by the esterases present in the organism, is represented by the preparation of capsules for subcutaneous implantation of medicaments or microcapsules to be administered by injection, for example by subcutaneous or intramuscular route.

Of great importance is also the preparation of microcapsules containing the new esters, a problem-free method for their use, which up till now has been very limited, for the reasons explained above, and which opens up a whole new area of application where a retard effect is to be achieved by injection.

Another application in the medical and surgical sectors of the new esters lies in the preparation of a wide variety of solid inserts such as plates, discs, sheets, etc. replacing the metal or synthetic plastic ones currently in use, in cases calling for temporary inserts to be removed after a certain length of time. Preparations containing animal collagen, being of a proteic nature, often give rise to unpleasant side effects, such as inflammation or rejection. In the case of the esters of the present invention, this danger is overcome.

Another application in the fields of medicine and surgery of the new esters according to the present invention is represented by preparations in expandable material, especially in the form of sponges, for the medication of injuries or various types of lesion.

The esterified carboxymethyl-polysaccharides of the present invention are extremely suitable, thanks to their viscosity in aqueous solutions, for the preparation of gels which can be widely used in the food industry, for example for the manufacture of ice creams, puddings and many other types of sweet dishes. They can also be used, thanks to their water retaining properties, for the conservation of frozen foods. Another property of the esters of carboxymethylderivatives of the above polysaccharides is their ability for form and to stabilize emulsions and they can therefore also serve in the food industry for the preparation of seasonings and for the stabilization of many drinks such as beer or fruit juices, sauces and syrups.

The ease with which the esters of the present invention form films and threads can be put to good use in the paper industry, for the manufacture of stickers or adhesive labels, in printing and in textile dyeing. As emulsifiers they can be used for the manufacture of polishes, anti-foam agents, lactics and as stabilizers in the ceramics and detergent industries.

Use of the new esters according to the present invention in the food industry presents various advantages over the polysaccharides usually used in the industry, for example alginic acid which has a tendency to precipitate in acid conditions. In the presence of calcium ions too the insoluble products constituted by calcium alginate may become separated, and for this reason the use of alkaline alginates is compromised whenever they are intended for use in liquids containing the abovesaid ions, for example in products containing milk or its derivatives. For this reason alkaline alginates were substituted by glycol esters of alginic acid, particularly propyleneglycol ester. Glycol esters may however be toxic to a certain degree and their use must therefore be kept within certain limits. These drawbacks do not exist for example in the case of the esters of monovalent alcohols of the present invention, which can be used preferably for the preparation of the abovesaid food additives. Also regarding the other abovesaid uses, the new polysaccharide esters open up a choice of surrogates which are an improvement on the products already in use. From the following list of alcohols, which can be used as esterifying components for carboxymethylpolysaccharides which are the basis of the present invention, those suitable for the use in question should be chosen. Thus for example for all uses 1) - 9) in the abovesaid sectors of industry alcohols of the aliphatic series with a low or medium number of carbon atoms should be preferred, or also simple heterocyclic alcohols or araliphatic

alcohols. The cycloaliphatic alcohols, in particular terpene alcohols should be used preferably for cosmetic products. As for the alcohols for use in the medicaments or pharmaceutical preparations described above, they are those to be considered as therapeutically active esterifying components, for example steroid or vitamin alcohols.

Alcohols of the aliphatic series to be used as esterifying components of the carboxy groups of carboxymethyl derivatives according to the various aspects of the present invention are those with a maximul of 34 carbon atoms, which may be saturated or unsaturated and which may possibly also be substituted by other free functional or functionally modified groups, such as amino, hydroxy, aldehydo, keto, mercapto, carboxy groups or by groups derived from these, such as hydrocarbyl or dihydrocarbylamino groups (hereafter the term "hydrocarbyl" should be taken to mean not only monovalent radicals of hydrocarbons for example of the C_nH_{2n+1} type, but also bivalent or trivalent radicals, such as "alkylenes" - C_nH_{2n} - or "alkylidenes" = C_nH_{2n}), ether or ester groups, acetal or ketal groups, thioether or thioester groups, and esterified carboxy groups or carbamidic groups perhaps substituted by one or two hydrocarbyl groups, by nitrile groups or by halogens.

In the abovesaid groups containing hydrocarbyl radicals these are preferably inferior aliphatic radicals, for example alkyls, with a maximum of 6 carbon atoms. Such alcohols may also be interrupted in the carbon atom chain by heteroatoms, such as oxygen, nitrogen and sulfur atoms.

It is preferable to choose alcohols substituted with one or two of the abovesaid functional groups.

Alcohols of the abovesaid group to be used preferably within the scope of the present invention are those with a maximum of 12 and especially 6 carbon atoms and in which the hydrocarbyl radicals in the abovesaid amino, ether, ester, thioether, thioester, aceto, ketal groups represent alkyl groups with a maximum of 4 carbon atoms, and also in the esterified carboxy or substituted carbamidic groups the hydrocarbyl groups are alkyls with the same number of carbon atoms, and in which the amino or carbamidic groups may be alkylene amino or alkylene carbamidic groups with a maximum of 8 carbon atoms. Of these alcohols, special mention should be made of those which are saturated and unsubstituted such as for example methyl, ethyl, propyl, isopropyl alcohols, n-butyl, isobutyl, tertbutyl alcohols, amyl alcohols, pentyl, hexyl, octyl, nonyl and dodecyl alcohols and above all those with a linear chain, such as n-octyl alcohol or n-dodecyl alcohol. Among the substituted alcohols of this group are bivalent alcohols such as ethylene glycol, popylene glycol or butylene glycol, trivalent alcohols such as glycerin, aldehydo-alcohols such as tartronic alcohol, carboxy alcohols such as lactic acid, for example α-oxypropionic acid, glycolic acid, malic acid, tartaric acids, citric acid, aminoalcohols, such as aminoethanol, aminopropanol, n-aminobutanol and their dimethylated and diethylated derivatives in the amino function, choline, pyrrolidinylethanol, piperidinylethanol, piperazinylethanol and the corresponding derivatives of n-propyl n-butyl alcohols, monothioethylenglycol and its alkyl derivatives, for example the ethylate derivative in the mercapto function.

Among the saturated superior aliphatic alcohols are for example cetyl alcohol and myricyl alcohol, but especially important for the aims of the present invention are unsaturated superior alcohols with one or two double bonds, such as especially those contained in many essential oils and having affinity with terpenes, for example citronellol, geraniol, nerol, nerolidol, linalool, farnesol, phytol. Of the inferior unsaturated alcohols, allyl alcohol and propargyl alcohol should be considered.

The araliphatic alcohols are those with one single benzene residue and in which the aliphatic chain has a maximum of 4 carbon atoms and in which the benzene residue may be substituted by between 1 and 3 methyl or hydroxy groups or by halogen atoms, especially by chlorine, bromine, iodine, and in which the aliphatic chain may be substituted by one or more functions chosen from the group constituted by free or mono or dimethylated amino groups or by pyrrolidine or piperidine groups. Of such alcohols special mention should be made of benzyl alcohol and phenethyl alcohol.

The alcohols of the cycloaliphatic or aliphatic-cycloaliphatic or heterocyclic series respectively derive from mono- or polycyclic hydrocarbons with a maximum of 34 carbon atoms and are unsubstituted or substituted by one or more functional groups chosen from the group formed by amino, hydroxy, mercapto, aldehydo, keto, carboxy, hydrocarbyl and dihydrocarbylamino, ether, ester, thioether, thioester, acetal, ketal, carbalkoxy, carbamidic and substituted carbamidic groups by one or two alkyl groups with the hydrocarbyl radicals in these functionally modified groups having a maximum of 6 carbon atoms, and which may be interrupted in the carbon atom chain by heteroatoms chosen from the group forced by - O -,

- S -, and which may have one or more bonds, including aromatic structures.

Alcohols of the cycloaliphatic or aliphatic cycloaliphatic series derive from mono or polycyclic hydrocarbons and have a maximum of 34 carbon atoms. Among the alcohols derived from single-ringed cyclic hydrocarbons, special mention should be made of those with a maximum of 12 carbon atoms, the rings having preferably between 5 and 7 carbon atoms, which may be substituted for example by between one and three inferior alkyl groups, such as methyl, ethyl, propyl or isopropyl groups. As specific alcohols of this group we can mention cyclohexanol, cyclohexanediol, 1,2,3-cyclohexanetriol and 1,3,5-cyclohexanetriol (phloroglucitol), inositol, and then the alcohols which derive from p-menthane, such as carvomenthol, menthol, α and γ -terpineol, 1-terpineol, 4-terpineol and piperitol, or the mixture of these alcohols known as "terpineol", 1,4-and 1,8-terpin. Of the alcohols deriving from hydrocarbons with condensed rings, for example those of the group including thujane, pinane or camphane, we can mention thujanol, sabinol, pinol hydrate, D and L-borneol and D and L-isoborneol.

Polycyclic cycloaliphatic aliphatic alcohols to be used for the esters of the present invention are sterols, cholic acids and steroids, such as sexual hormones and their synthetic analogues and particularly corticosteroids and their derivatives. Thus for example the following can be used: cholesterol, dihydrocholesterol, epidihydrocholesterol, corpostanol, epicoprostanol, sitosterol, stigmasterol, ergosterol, cholic acid, deoxycholic acid, lithocholic acid, estriol, estradiol, equilenin, equilin and their alkyl derivatives, as well as their ethynyl and propynyl derivatives in position 17, for example 17-α-ethynyl-estradiol or 7-α-methyl-17-α-ethynylestradiol, pregnenolone, pregnandiol, testosterone and its derivatives, such as 17-α-methyltestosterone, 1,2-dehydrotestosterone and 17-α-methyl-1,2-dehydrotestosterone, alkynyl derivatives in position 17 of testosterone and 1,2-dehydrotestosterone, such as 17-α-ethynyltestosterone, 17-α-propynyltestosterone, norgestrel, hydroxyprogesterone, corticosterone, deoxycorticosterone, 19-nortestosterone, 19-nor-17-α-methyltestosterone and 19-nor-17-α-ethynyltestosterone, cortisone, hydrocortisone, prednisone, prednisolone, fludrocortisone, dexamethasone, betamethasone, paramethasone, flumethasone, fluocinolone, fluprednylidene, clobetasol, beclomethasone, aldosterone, deoxycorticosterone, alfaxalone, alfadolone, bolasterone and antihormones such as cyproterone.

Useful esterifying components for the esters of the present invention are genins (aglycons) of cardioactive glycosides, such as digitoxigenin, gitoxygenin, digoxygenin, strophanthidin, tigogenin and saponins.

Other alcohols for use according to the invention are vitamin alcohols, such as axerophthol, vitamins D_2 and D_3, aneurine, lactoflavine, ascorbic acid, riboflavine, thiamine, pantothenic acid.

Heterocyclic alcohols to be used are furfuryl alcohol, alkaloids and derivatives such as atropine, scopolamine, cinchonine, cinchonidine, quinine, morphine, codeine, nalorphine, N-butylscopolammonium bromide, ajmaline; phenylethylamines such as ephedrine, isoproterenol, epinephrine; phenothiazine drugs such as perphenazine, pipothiazine, carphenazine, homophenazine, acetophenazine, fluphenazine, N-hydroxyethylpromethazine chloride; thioxanthene drugs such as flupenthixol and clopenthixol; anticonvulsivants such as meprophendiol, antipsychotics such as opipramol; antiemetics such as oxypendyl; analgesics such as carbetidine and phenoperidine and methadol; hypnotics such as etodroxizine; anorexics such as benzyhydrol and diphemethoxidine; minor tranquilizers such as hydroxyzine; muscle relaxants such as cinnamedrine, diphylline, mephenesin, methocarbamol, chlorphenesin, 2,2-diethyl-1,3propanediol, guaifenesin, idricilamide; coronary vasodialtors such as dipyridamole and oxyfedrine; adrenergic blockers such as propanolol, timolol, pindolol, bupranolol, antenolol, metoprolol, practolol; antineoplastics such as 6-azauridine, cytarabine, floxuridine; antibiotics such as chloroamphenicol, thiamphenicol, erythromycin, oleandomycin, lincomycin; antivirals such as iodoxuridine; peripheral vasodilatators such as isonicotiny alcohol; carbonic anhydrase inhibitors such as sulocarbilate; antiasthmatics and antiinflammatories such as tiaramide; sulfamidics such as 2-p-sulfanylanilinoethanol.

According to the procedure of the present invention carboxymethyl-polysaccharide esters may be prepared to advantage by starting with quaternary ammonium salts of carboxymethyl-polysaccharide acid with an etherifying agent in an organic solvent, preferably aprotic, such as inferior alkyl dialkylsulfoxides, especially dimethylsulfoxide, and inferior alkyl dialkylamides of aliphatic acids, such as dimethyl or diethyl formamide or dimethyl or diethyl acetamide.

Reaction is carried out within a temperature range of 0° to 100°, and especially between 25° and 75°, for example at about 30°. Esterification is effected preferably by gradually adding the esterifying agent to the abovesaid ammonium salt dissolved in one of the abovesaid solvents, for example in dimethylsulfoxide. The alkylating agents can be those mentioned above, especially hydrocarbyl halides, for example alkyl halides. As starting quaternary ammonium salts it is preferable to use inferior tetraalkylammonium salts, with the alkyl groups having preferably between 1 and 6

carbon atoms. Mainly, the tetrabutylammonium salt of carboxymethylpolysaccharide is used. These quaternary ammonium salts can be prepared by reacting a metal salt of acidic polysaccharide, preferably one of those mentioned above, especially sodium or potassium salt, in aqueous solution with a salified sulfonic resin with the quaternary ammonium base. Tetraalkylammonium salt of acidic polysaccharide can be obtained by freeze-drying the eluate.

The starting ammonium salts are soluble in the abovesaid aprotic solvents, so esterification of acidic polysaccharide is very easy and gives abundant yields. By this procedure alone therefore it is possible to exactly dose the number of carboxy groups of acidic polysaccharide to be esterified.

One variation of the previously described procedure consists in reacting potassium salt or sodium salt of acidic polysaccharide, suspended in suitable solvent, such as dimethylsulfoxide, with a suitable alkylating agent in the presence of catalyzing quantities of a quaternary ammonium salt, such as tetrabutylammonium iodide.

The procedure makes it possible to obtain, as we have already said, the total esters of acidic polysaccharide, and also of substituted alcohols, such as glycols, which have till now been inaccessible.

Of the new products of the present invention particular emphasis should be placed on the esters described above and those featuring in the following illustrative examples.

The present invention also includes modifications in the preparation procedure, new esters and their salts, in which a procedure is interrupted at any one stage or in which it is begun with an intermediate compound and the remaining stages are carried out, or in which the starting products are formed in situ.

The invention is illustrated by the following examples, without however being limited in any way by the same.

EXAMPLE 1: PREPARATION OF THE TETRABUTYLAMMONIUM SALT OF CARBOXYMETHYLCHITIN

10 mEq. of sodium salt of a carboxylmethylchitin with a substitution rate of 0.99, prepared according to Trujillo (Carbohydrate Res. 7, 483 (1968), corresponding to 2.85g of dry compound, are solubilized in 300ml of distilled water. The solution is then passed through a thermostatic column regulated at 4 °C and containing 15ml of sulfonic resin (Dowex 50 x 8) in the form of tetrabutylammonium.
The sodium-free eluate is freeze-dried.
Yield: 5.05 g.

EXAMPLE 2: PREPARATION OF THE ETHYL ESTER OF A CARBOXYMETHYLCHITIN WITH A SUBSTITUTION RATE OF 0.99

5.05 g (10 mEq) of tetrabutylammonium salt of a carboxymethylchitin with a substitution rate of 0.99 are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
1.56 g (10 mEq) of ethyl iodide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 2.90 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 3.41 mEq/g (theoretical 3.43).

EXAMPLE 3: PREPARATION OF THE ISOPROPYL ESTER OF A CARBOXYMETHYLCHITIN WITH A SUBSTITUTION RATE OF 0.99

5.05 g (10 mEq) of tetrabutylammonium salt of a carboxymethylchitin with a substitution rate of 0.99 are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
1.70 g (10 mEq) of 2-iodopropane are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 3.0 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 3.23 mEq/g (theoretical 3.28).

EXAMPLE 4: PREPARATION OF THE BENZYL ESTER OF A CARBOXYMETHYLCHITIN WITH A SUBSTITUTION RATE OF 0.99

5.05 g (10 mEq) of tetrabutylammonium salt of a carboxymethylchitin with a substitution rate of 0.99 are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
1.71 g (10 mEq) of benzyl bromide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and

washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 3.5 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 2.81 mEq/g (theoretical 2.83).

EXAMPLE 5: PREPARATION OF THE p-BROMO BENZYL ESTER OF A CARBOXYMETHYLCHITIN WITH A SUBSTITUTION RATE OF 0.99

5.05 g (10 mEq) of tetrabutylammonium salt of a carboxymethylchitin with a substitution rate of 0.99 are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
2.5 g (10 mEq) of p-bromobenzyl bromide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 4.29 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 2.29 mEq/g (theoretical 2.31).

EXAMPLE 6: PREPARATION OF THE MYRISTYL ESTER OF A CARBOXYMETHYLCHITIN WITH A SUBSTITUTION RATE OF 0.99

5.05 g (10 mEq) of tetrabutylammonium salt of a carboxymethylchitin with a substitution rate of 0.99 are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
2.77 g (10 mEq) of myristylbromide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 4.57 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 2.16 mEq/g (theoretical 2.18).

EXAMPLE 7: PREPARATION OF THE TETRABUTYLAMMONIUM SALT OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND LOW VISCOSITY

10 mEq of sodium salt of a carboxymethylcellulose with a substitution rate of 0.75 and low viscosity (30 mPa.s, solution at 2% in distilled water at 20 °C by Hoppler viscosimeter), corresponding to 2,96 g of dry compound, are solubilized in 300 ml of distilled water. The solution is then passed through a thermostatic column regulated at 4 °C and containing 15 ml of sulfonic resin (Dowex 50 x 8) in the form of tetrabutylammonium.
The sodium-free eluate is freeze-dried.
Yield: 5.05 g.

EXAMPLE 8: PREPARATION OF THE ETHYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND LOW VISCOSITY

5.15 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 0.75 and low viscosity, prepared as in example 7, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
1.56 g (10 mEq) of ethyl iodide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 2.91 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 3.30 mEq/g (theoretical 3.31).

EXAMPLE 9: PREPARATION OF THE ISOPROPYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND LOW VISCOSITY

5.15 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 0.75 and low viscosity, prepared as in example 7, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
1.70 g (10 mEq) of 2-iodopropane are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum

Yield: 3.02 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 3.12 mEq/g (theoretical 3.16).

EXAMPLE 10: PREPARATION OF THE ISOPROPYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND LOW VISCOSITY

5.15 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 0.75 and low viscosity, prepared as in example 7, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
1.71 g (10 mEq) of benzyl bromide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 3.54 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 2.70 mEq/g (theoretical 2.74).

EXAMPLE 11: PREPARATION OF THE p-BROMOBENZYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND LOW VISCOSITY

5.15 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 0.75 and low viscosity, prepared as in example 7, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
2.5 g (10 mEq) of p-bromobenzyl-bromide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 4.35 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 2.25 mEq/g (theoretical 2.28).

EXAMPLE 12: PREPARATION OF THE MYRISTYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND LOW VISCOSITY

5.15 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 0.75 and low viscosity, prepared as in example 7, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
2.77 g (10 mEq) of myristyl bromide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 4.61 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 2.12 mEq/g (theoretical 2.15).

EXAMPLE 13: PREPARATION OF THE TETRABUTYLAMMONIUM SALT OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND MEDIUM VISCOSITY

10 mEq of sodium salt of a carboxymethylcellulose with a substitution rate of 0.75 and medium viscosity (30 mPa.s, solution at 2% in distilled water at 20 °C by Hoppler viscosimeter), corresponding to 2,96 g of dry compound, are solubilized in 300 ml of distilled water. The solution is then passed through a thermostatic column regulated at 4 °C and containing 15 ml of sulfonic resin (Dowex 50 x 8) in the form of tetrabutylammonium.
The sodium-free eluate is freeze-dried.
Yield: 5.00 g.

EXAMPLE 14: PREPARATION OF THE ETHYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND MEDIUM VISCOSITY

5.15 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 0.75 and medium viscosity, prepared as in example 13, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
1.56 g (10 mEq) of ethyl iodide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum

Yield: 2.93 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 3.24 mEq/g (theoretical 3.31).

EXAMPLE 15: PREPARATION OF THE ISOPROPYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND MEDIUM VISCOSITY

5.15 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 0.75 and medium viscosity, prepared as in example 13, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
1.7 g (10 mEq) of 2-iodopropane are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 3.1 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 3.11 mEq/g (theoretical 3.16).

EXAMPLE 16: PREPARATION OF THE BENZYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND MEDIUM VISCOSITY

5.15 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 0.75 and medium viscosity, prepared as in example 13, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
1.71 g (10 mEq) of benzyl bromide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 3.04 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 2.70 mEq/g (theoretical 2.74).

EXAMPLE 17: PREPARATION OF THE p-BROMO BENZYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND MEDIUM VISCOSITY

5.15 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 0.75 and medium viscosity, prepared as in example 13, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
2.5 g (10 mEq) di p-bromobenzyl bromide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 4.32 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication.

EXAMPLE 18: PREPARATION OF THE MYRISTYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND MEDIUM VISCOSITY

5.15 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 0.75 and medium viscosity, prepared as in example 13, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
2.77 g (10 mEq) of myristyl bromide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 4.61 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 2.12 mEq/g (theoretical 2.15).

EXAMPLE 19: PREPARATION OF THE TETRABUTYLAMMONIUM SALT OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND HIGH VISCOSITY

10 mEq of sodium salt of a carboxymethylcellulose with a substitution rate of 0.75 and high viscosity (6000 mPa.s, solution at 2% in distilled water at 20 °C by Hoppler viscosimeter), corre-

sponding to 2.96 g of dry compound, are solubilized in 300 ml of distilled water. The solution is then passed through a thermostatic column regulated at 4 °C and containing 15 ml of sulfonic resin (Dowex 50 x 8) in the form of tetrabutylammonium.
The sodium-free eluate is freeze-dried.
Yield: 4.95 g.

EXAMPLE 20: PREPARATION OF THE ETHYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND HIGH VISCOSITY

5.15 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 0.75 and high viscosity, prepared as in example 19, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
1.56 g (10 mEq) of ethyl iodide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 2.91 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 3.30 mEq/g (theoretical 3.31).

EXAMPLE 21: PREPARATION OF THE ISOPROPYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND HIGH VISCOSITY

5.15 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 0.75 and high viscosity, prepared as in example 19, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
1.7 g (10 mEq) of 2-iodopropane are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 3.02 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 3.07 mEq/g (theoretical 3.16).

EXAMPLE 22: PREPARATION OF THE BENZYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND HIGH VISCOSITY

5.15 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 0.75 and high viscosity, prepared as in example 19, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
1.71 g (10 mEq) of benzyl bromide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 3.46 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 2.72 mEq/g (theoretical 2.74).

EXAMPLE 23: PREPARATION OF THE p-BROMO BENZYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND HIGH VISCOSITY

5.15 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 0.75 and high viscosity, prepared as in example 19, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
2.5 g (10 mEq) of p-bromobenzyl bromide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 4.28 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 2.26 mEq/g (theoretical 2.28).

EXAMPLE 24: PREPARATION OF THE MYRISTYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 0.75 AND HIGH VISCOSITY

5.15 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of

0.75 and high viscosity, prepared as in example 19, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
2.77 g (10 mEq) of myristyl bromide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 4.54 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 2.11 mEq/g (theoretical 2.15).

EXAMPLE 25: PREPARATION OF THE TETRABUTYLAMMONIUM SALT OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 1.0 AND MEDIUM VISCOSITY

10 mEq of sodium salt of a carboxymethylcellulose with a substitution rate of 1.0 and medium viscosity (200 mPa.s, solution at 2% in distilled water at 20 °C by Hoppler viscosimeter), corresponding to 2,42 g of dry compound, are solubilized in 300 ml of distilled water. The solution is then passed through a thermostatic column regulated at 4 °C and containing 15 ml of sulfonic resin (Dowex 50 x 8) in the form of tetrabutylammonium.
The sodium-free eluate is freeze-dried.
Yield: 4.6 g.

EXAMPLE 26: PREPARATION OF THE ETHYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 1.0 AND MEDIUM VISCOSITY

4.62 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 1.0 and medium viscosity, prepared as in example 25, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
1.56 g (10 mEq) of ethyl iodide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 2.44 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 4.0 mEq/g (theoretical 4.03).

EXAMPLE 27: PREPARATION OF THE ISOPROPYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 1.0 AND MEDIUM VISCOSITY

4.62 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 1.0 and medium viscosity, prepared as in example 25, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
1.70 g (10 mEq) of 2-iodopropane are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 2.58 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 3.69 mEq/g (theoretical 3.81).

EXAMPLE 28: PREPARATION OF THE BENZYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 1.0 AND MEDIUM VISCOSITY

4.62 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 1.0 and medium viscosity, prepared as in example 25, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
1.71 g (10 mEq) of benzyl bromide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 3.05 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 3.15 mEq/g (theoretical 3.22).

EXAMPLE 29: PREPARATION OF THE p-BROMOBENZYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 1.0 AND MEDIUM VISCOSITY

4.62 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 1.0 and medium viscosity, prepared as in example

25, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
2.5 g (10 mEq) of p-bromobenzyl bromide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 3.85 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication.

EXAMPLE 30: PREPARATION OF THE MYRISTYL ESTER OF A CARBOXYMETHYLCELLULOSE WITH A SUBSTITUTION RATE OF 1.0 AND MEDIUM VISCOSITY

4.62 g (10 mEq) of tetrabutylammonium salt of a carboxymethylcellulose with a substitution rate of 1.0 and medium viscosity, prepared as in example 25, are solubilized in 200 ml of DMSO at 25 °C under agitation and in absolutely dry conditions.
2.77 g (10 mEq) of myristyl bromide are added and the solution is agitated overnight at 30 °C.
1000 ml of ethyl acetate are slowly added drop by drop, the precipitate is separated by filtration and washed 3 times with 100 ml of ethyl acetate, then dried in high vacuum
Yield: 4.12 g.
Quantitative determination of the ester groups is carried out according to the saponification method described on pages 169-172 of "Quantitative Organic Analysis Via Functional Groups" 4th Edition, John Wiley and Sons Publication and shows an ester group content of 2.36 mEq/g (theoretical 2.4).

As discussed above, the new polysaccharide esters of the invention are useful for the preparation of pharmaceutical formulations and new medical articles.

The following preparations exemplify the medical articles according to the invention containing the esters of the invention.

Example 31 - Preparation of films using esters of carboxymethylcellulose.

A solution is prepared in dimethylsulfoxide of the n-propyl ester of carboxymethylcellulose.

By means of a stratifier, a thin layer of solution is spread on a glass sheet; the thickness must be 10 times greater than the final thickness of the film. The glass sheet is immersed in ethanol which absorbs the dimethylsulfoxide but does not solubilize the carboxymethylcellulose ester which becomes solid. The film is detached from the glass sheet, is repeatedly washed with ethanol, then with water and then again with ethanol.

The resulting sheet is dried in a press for 48 hours at 30 °.

Example 32 - Preparation of threads using esters of carboxymethylcellulose.

A solution is prepared in dimethylsulfoxide of the benzyl ester of carboxymethylcellulose. The solution thus obtained is pressed by means of a pump through a threader with 0.5 mm holes.

The threader is immersed in ethanol/dimethylsulfoxide 80:20 (this concentration is kept constant by continuous addition of ethanol); when the solution in dimethylsulfoxide is soaked in this way it tends to lose most of the dimethylsulfoxide and the thread solidifies.

The thread is stretched while it still has a content of dimethylsulfoxide, is then repeatedly stretched and washed with ethanol. The thread is dried in nitrogen current.

Example 33 - Preparation of a spongy material made with esters of carboxymethylcellulose.

1 g of benzyl ester of carboxymethylcellulose in which all the carboxylic groups are esterified (obtained for example as described in Example 22) are dissolved in 5 ml of dimethylsulfoxide. To each 10 ml of solution prepared, a mixture of 31.5 g of sodium chloride with a degree of granularity corresponding to 300 μ, 1.28 g of sodium bicarbonate and 1 g of citric acid is added and the whole is homogenized in a mixer.

The pasty mixture is stratified in various ways, for instance by means of a mange consisting of two rollers which turn opposite each other at an adjustable distance between the two. Regulating this distance the paste is passed between the rollers together with a strip of silicone paper which acts as a support to the layer of paste thus formed. The layer is cut to the desired dimensions of length and breadth, removed from the silicone, wrapped in filter paper and emerged in a suitable solvent, such as water. The sponges thus obtained are washed with a suitable solvent such as water and possibly sterilized with gamma rays.

Example 34 - Preparation of a spongy material made with esters of carboxymethylcellulose.

In the manner described in Example 33, it is possible to prepare spongy materials with other carboxymethylcellulose esters. In the place of dimethylsulfoxide it is possible to use, if desired, any other solvent capable of dissolving the chosen

ester. In the place of sodium chloride it is possible to use any other solid compound which is insoluble in the solvent used to dissolve the carboxymethylcellulose ester, but which is however soluble in the solvent used to precipitate the carboxymethylcellulose ester after the above mentioned mechanical treatment, and finally which has the correct degree of granularity to obtain the type of pores desired in the sponge material.

In the place of sodium bicarbonate and citric acid it is possible to use other couples of similar compounds, that is, compounds which react to each other in suspension or solution of the solvent used to dissolve carboxymethylcellulose in such a way as to form a gas, such as carbon dioxide, which has the effect of producing a less compact spongy material. In this way it is possible to use, in the place of sodium bicarbonate, other bicarbonates or alkaline or alkaline earth carbonates and in the place of citric acid other acids in solid form, such as tartaric acid.

Claims

1. Total esters of acidic polysaccharides chosen from the group formed by carboxymethylcellulose, carboxymethyl starch and carboxymethylchitin wherein the carboxy groups of said polysaccharide are esterfied with an alcohol of the aliphatic, araliphatic, cycloaliphatic and heterocyclic series, whereby the alcohols of the aliphatic series have a maximum of 34 carbon atoms and are unsubstituted or substituted by one or two functional groups chosen from the groups formed by amino, hydroxy, mercapto, aldehydo, keto, carboxy, hydrocarbyl and dihydrocarbylamino, ether, ester, thioether, thioester, acetal, ketal, carbalkoxy groups, carbamidic and substituted carbamidic groups by one or two alkyl groups with the hydrocarbyl radicals in these functionally modified groups having a maximum of 6 carbon atoms, and in which such alcohols of the aliphatic series may be interrupted in the carbon atom chain by heteroatoms chosen from the group formed by oxygen, sulfur and nitrogen, the alcohols of the araliphatic series are those with only one benzene residue and in which the aliphatic chain has a maximum of 4 carbon atoms and in which the benzene residue may be substituted by between 1 and 3 methyl or hydroxy groups, by halogen atoms, and in which the aliphatic chain may be substituted by one or two functions chosen from the group formed by free amino or mono- or diethyl groups or by pyrrolidine or piperidine groups, and the alcohols of the cycloaliphatic or aliphaticcycloaliphatic or heterocyclic series respectively derive from mono- or polycyclic hydrocarbons with a maximum of 34 carbon atoms and are unsubstituted or substituted by one or more functional groups chosen from the group formed by amino, hydroxy, mercapto, aldehydo, keto, carboxy, hydrocarbyl and dihydrocarbylamino, ether, ester, thioether, thioester, acetal, ketal, carbalkoxy, carbamidic and substituted carbamidic groups by one or two alkyl groups with the hydrocarbyl radicals in these functionally modified groups having a maximum of 6 carbon atoms, and which may be interrupted in the carbon atom chain by heteroatoms chosen from the group formed by - O -,

- S -, and which may have one or more bonds, including aromatic structures.

2. Esters of acidic polysaccharides according to claim 1, wherein said alcohol of the aliphatic series has a maximum of 12 carbon atoms; said hydrocarbyl radicals have a maximum or 4 carbon atoms; and wherein said amino or substituted carbamidic groups may also be alkyleneamino groups or alkylenecarbamidic groups with a maximum of 8 carbon atoms.

3. Esters of acidic polysaccharides according to claim 2, wherein said alcohol is ethyl, propyl, isopropyl, n-butyl, isobutyl, tert-butyl alcohols, an amyl, pentyl, hexyl or octyl alcohol.

4. Esters of acidic polysaccharides according to claim 2, wherein said alcohol is glycerin.

5. Esters of acidic polysaccharides according to claim 2, wherein said esterifying alcohol is tartronic alcohol, lactic acids, glycolic acid, malic acid, a tartaric acid or citric acid.

6. Esters of acidic polysaccharides according to claim 2, wherein the esterifying alcohol is aminoethanol, aminopropanol, n-aminobutanol or dimethyl or diethyl derivatives thereof in the amino function, choline, pyrrolidinylethanol, piperidinylethanol, piperazinylethanol or the corresponding derivatives of n-propyl or n-butyl alcohols, or monothioethyleneglycol or its lower alkylderivatives in the mercapto function.

7. Esters of acidic polysaccharides according to claim 2, wherein the esterifying alcohol component is a higher aliphatic alcohol chosen from

the group formed by cetyl, myricyl alcohols, citronellol, geraniol, nerol, nerolidol, linalool, farnesol, and phytol.

8. Esters of acid polysaccharides according to claim 1, wherein the araliphatic alcohol is chosen from the group formed by benzyl alcohol, phenethyl alcohol, ephedrine and adrenaline.

9. Esters of acidic polysaccharides according to claim 1, in which the cyclic alcohols are monocyclic having a maximum of 12 carbon atoms and the ring having between 5 and 7 carbon atoms possibly substituted by between one and three inferior alkyl groups.

10. Esters of acidic polysaccharides according to claim 1, in which the polycyclic alcohols are sterines, cholic acids, or steroid alcohols.

11. Esters of acidic polysaccharides according to claim 1, in which the alcohols are chosen from the group formed by alkaloids, phenethylamines, phenothiazine drugs, thioxanthenes and sulfamidics.

12. An ester of an acidic polysaccharide according to claim 1, wherein said ester is a compound chosen from the group formed by an ethyl, isopropyl, benzyl, p-bromo-benzyl, and mirystyl ester of carboxymethylchitin.

13. An ester of an acidic polysaccharide according to claim 1, wherein said ester is a compound chosen from the group formed by an ethyl, isopropyl, benzyl, p-bromo-benzyl, and mirystyl ester of carboxymethylcellulose.

14. A pharmaceutical preparation containing as an active ingredient an ester according to any one of claims 1-12.

15. A pharmaceutical preparation according to claim 14 for parenteral administration.

16. A pharmaceutical preparation or medicament which comprises:

1) a pharmacologically active substance or an association of pharmacologically active substances; and

2) a vehicle comprised of a total ester according to claims 1 - 13

17. A pharmaceutical preparation or medicament which comprises a total ester according to claims 1 - 13 in which at least one of said alcohols is therapeutically active.

18. A pharmaceutical preparation or medicament according to any one of claims 16 and 17, in which the active substance is for topical use.

19. Therapeutic use of total esters of acidic polysaccharides chosen from the group formed by carboxymethylcellulose, carboxymethyl starch and carboxymethylchitin with alcohols of the aliphatic, araliphatic, cycloaliphatic and heterocyclic series according to claim 1.

20. Use of an ester of an acidic polysaccharide chosen from the group formed by carboxymethylcellulose, carboxymethyl starch and carboxymethylchitin with alcohols of the aliphatic, araliphatic, cycloaliphatic and heterocyclic series according to claim 1 in the cosmetic field.

21. Use of an ester of an acidic polysaccharide chosen from the group formed by carboxymethylcellulose, carboxymethyl starch and carboxymethylchitin with alcohols of the aliphatic, araliphatic, cycloaliphatic and heterocyclic series according to claim 1 in one of the following fields:

1) food industry
2) paper industry
3) adhesive products
4) printing
5) textile dyeing
6) preparation of sanitary, medical and surgical articles
7) galenics, for the preparation of capsules and microcapsules
8) biology, for the immobilization of enzymes
9) emulsifiers for glazes, polishes, antifoam agents, lactics and stabilizers in the ceramics and detergent industries.

22. Sanitary and surgical articles containing an ester of an acidic polysaccharide chosen from the group formed by carboxymethylcellulose, carboxymethyl starch and carboxymethylchitin with alcohols of the aliphatic, araliphatic, cycloaliphatic and heterocyclic series according to claim 1.

23. Sanitary and surgical articles according to claim 22, which comprises a total ester of an acidic polysaccharide according to any one of claims 1-13.

24. Sanitary and surgical articles according to one of claims 22-23, in the form of a film.

25. Sanitary and surgical articles according to one off claims 22-23, in the form of a thread.

26. Sanitary and surgical articles according to one of claims 22-23, in the form of suture threads for surgical operations.

27. Sanitary and surgical articles according to one of claims 22-23, in the form of films for use as artificial skin in dermatology.

28. Sanitary and surgical articles according to one of claims 22-23, in the form of capsules for subcutaneous implant of medicaments.

29. Sanitary and surgical articles according to one of claims 22-23, in the form of microcapsules for subcutaneous, intramuscular or intraveneous injection.

30. Sanitary and surgical articles according to one of claims 22-23, in the form of solid inserts to be removed after a certain period of time.

31. Sanitary and surgical articles according to one of claims 22-23, in the form of sponges for the medication of injuries and lesions.

32. A process for the preparation of a total ester of acidic polysaccharides according to claims 1 to 13 which comprises treating a quaternary ammonium salt of a polysaccharide with an etherifying agent in an aprotic solvent at a temperature of 0 to 100 ° C.

33. A process according to claim 32, wherein said solvent is dimethylsulfoxide.

34. A process according to claim 32, wherein said quaternary ammonium salt is a lower tetraalkylammonium salt.

35. A process for the preparation of a pharmaceutical preparation according to claims 14 to 18 which comprises combining the active ingredient with a pharmaceutically acceptable vehicle.

Patentansprüche

1. Vollständige Ester saurer Polysaccharide, ausgewählt aus Carboxymethylcellulose, Carboxymethylstärke und Carboxymethylchitin, wobei die Carboxylgruppen dieser Polysaccharide verestert sind mit einem Alkohol der aliphatischen, araliphatischen, cycloaliphatischen und heterocyclischen Reihe, wobei die Alkohole der aliphatischen Reihe höchstens 34 Kohlenstoffatome besitzen und unsubstituiert sind oder substituiert sind mit einer oder zwei funktionellen Gruppen ausgewählt aus Amino-, Hydroxy-, Mercapto-, Aldehyd-, Keto-, Carboxyl-, Kohlenwasserstoff- und Dikohlenwasserstoffamino-, Ether-, Ester-, Thioether-, Thioester-, Acetal-, Ketal- und Carbalkoxygruppen, Carbamido- und mit einer oder zwei Alkylresten substituierten Carbamidogruppen, wobei die Kohlenwasserstoffreste in diesen funktionell modifizierten Gruppen höchstens 6 Kohlenstoffatome besitzen und wobei die Kohlenstoffatomkette der Alkohole der aliphatische Reihen durch Heteroatome unterbrochen sein kann, ausgewählt aus Sauerstoff, Schwefel und Stickstoff, die Alkohole der araliphatischen Reihe nur einen Benzolrest besitzen, wobei die aliphatische Kette höchstens 4 Kohlenstoffatome besitzt und der Benzolrest mit 1 bis 3 Methyl- oder Hydroxylgruppen oder mit Halogenatomen substituiert sein kann, und wobei die aliphatische Kette mit einer oder zwei Funktionen substituiert sein kann, ausgewählt aus freien Aminogruppen oder Mono- oder Diethylgruppen oder durch Pyrrolidin- oder Piperidingruppen, und wobei die Alkohole der cycloaliphatischen, aliphatisch-cycloaliphatischen oder heterocyclischen Reihe von mono- oder polycyclischen Kohlenwasserstoffen mit höchstens 34 Kohlenstoffatomen stammen und unsubstituiert sind oder substituiert sind mit einer oder mehreren funktionellen Gruppen, ausgewählt aus Amino-, Hydroxy-, Mercapto-, Aldehyd-, Keto-, Carboxyl-, Kohlenwasserstoff- und Dikohlenwasserstoffamino-, Ether-, Ester-, Thioether-, Thioester-, Acetal-, Ketal-, Carbalkoxy-, Carbamidogruppen und Carbamidogruppen, die mit einer oder zwei Alkylresten substituiert sind, wobei die Kohlenwasserstoffreste in diesen funktionell modifizierten Gruppen höchstens 6 Kohlenstoffatome besitzen, und wobei die Kohlenstoffatomkette durch Heteroatome unterbrochen sein kann, ausgewählt aus - O -,

- S - und wobei diese eine oder mehrere Bindungen besitzen kann, einschließlich aromatischer Strukturen.

2. Ester saurer Polysaccharide nach Anspruch 1, wobei der Alkohol der aliphatischen Reihe höchstens 12 Kohlenstoffatome und die Kohlenwasserstoffreste höchstens 4 Kohlenstoffatome besitzen und wobei die Amino- oder

substituierten Carbamidogruppen auch Alkylenaminogruppen oder Alkylencarbamidogruppen mit höchstens 8 Kohlenstoffatomen sein können.

3. Ester der sauren Polysaccharide nach Anspruch 2, wobei der Alkohol Ethyl-, Propyl-, Isopropyl-, n-Butyl-, Isobutyl-, tert.-Butylalkohol, ein Amyl-, Pentyl-, Hexyl- oder Octylalkohol ist.

4. Ester der sauren Polysaccharide nach Anspruch 2, wobei der Alkohol Glycerin ist.

5. Ester der sauren Polysaccharide nach Anspruch 2, wobei der veresternde Alkohol Tartronalkohol, eine Milchsäure, Glykolsäure, Äpfelsäure, Weinsäure oder Citronensäure ist.

6. Ester der sauren Polysaccharide nach Anspruch 2, wobei der veresternde Alkohol Aminoethanol, Aminopropanol, n-Aminobutanol oder Dimethyl- oder Diethylderivate in der Aminofunktion davon ist, Cholin, Pyrrolidinylethanol, Piperidinylethanol, Piperazinylethanol oder die entsprechenden Derivate der n-Propyl- oder n-Butylalkohole ist, oder Monothioethylenglykol oder seine niederen Alkylderivate in der Mercaptofunktion.

7. Ester der sauren Polysaccharide nach Anspruch 2, wobei der veresternde Alkoholbestandteil ein höherer aliphatischer Alkohol ist, ausgewählt aus Cetyl- und Myricylalkoholen, Citronellol, Geraniol, Nerol, Nerolidol, Linalool, Farnesol und Phytol.

8. Ester der sauren Polysaccharide nach Anspruch 1, wobei der araliphatische Alkohol ausgewählt ist aus Benzylalkohol, Phenethylalkohol, Ephedrin und Adrenalin.

9. Ester der sauren Polysaccharide nach Anspruch 1, wobei die cyclischen Alkohole monocyclisch sind, höchstens 12 Kohlenstoffatome haben und der 5 bis 7 Kohlenstoffatome besitzende Ring mit 1 bis 3 Niederalkylresten substituiert sein kann.

10. Ester der sauren Polysaccharide nach Anspruch 1, wobei die polycyclischen Alkohole Sterine, Cholsäuren oder Steroidalkohole sind.

11. Ester der sauren Polysaccharide nach Anspruch 1, wobei die Alkohole ausgewählt sind aus Alkaloiden, Phenethylaminen, Phenothiazin-Wirkstoffen, Thioxanthenen und Sulfamiden.

12. Ester eines sauren Polysaccharids nach Anspruch 1, wobei der Ester eine Verbindung ist, ausgewählt aus einem Ethyl-, Isopropyl-, Benzyl-, p-Brombenzyl- und Myristylester von Carboxymethylchitin.

13. Ester eines sauren Polysaccharids nach Anspruch 1, wobei der Ester eine Verbindung ist, ausgewählt aus einem Ethyl-, Isopropyl-, Benzyl-, p-Brombenzyl- und Myristylester von Carboxymethylcellulose.

14. Arzneimittel, enthaltend als Wirkstoff einen Ester nach einem der Ansprüche 1 bis 12.

15. Arzneimittel nach Anspruch 14 zur parenteralen Verabreichung.

16. Arzneimittel oder Medikament, enthaltend:
1) eine pharmakologisch wirksame Substanz oder einen Zusammenschluß pharmakologisch wirksamer Substanzen, und
2) ein Vehikel, umfassend einen vollständigen Ester nach einem der Ansprüche 1 bis 13.

17. Arzneimittel oder Medikament, umfassend einen vollständigen Ester nach einem der Ansprüche 1 bis 13, wobei mindestens einer der Alkohole therapeutisch wirksam ist.

18. Arzneimittel oder Medikament nach Anspruch 16 oder 17, wobei die wirksame Substanz zur lokalen Anwendung ist.

19. Therapeutische Verwendung vollständiger Ester saurer Polysaccharide, ausgewählt aus Carboxymethylcellulose, Carboxymethylstärke und Carboxymethylchitin, mit Alkoholen der aliphatischen, araliphatischen, cycloaliphatischen und heterocyclischen Reihe nach Anspruch 1.

20. Verwendung eines Esters eines sauren Polysaccharids, ausgewählt aus Carboxymethylcellulose, Carboxymethylstärke und Carboxymethylchitin, mit Alkoholen der aliphatischen, araliphatischen, cycloaliphatischen und heterocyclischen Reihe nach Anspruch 1 im Kosmetikbereich.

21. Verwendung eines Esters eines sauren Polysaccharids, ausgewählt aus Carboxymethylcellulose, Carboxymethylstärke und Carboxymethylchitin, mit Alkoholen der aliphatischen, araliphatischen, cycloaliphatischen und heterocyclischen Reihe nach Anspruch 1 in einem der folgenden Bereiche:
1) Nahrungsmittelindustrie,

2) Papierindustrie,
3) Klebstoffe,
4) Druck,
5) Textilfärbung
6) Herstellung von sanitären, medizinischen und chirurgischen Artikeln,
7) Galenika, zur Herstellung von Kapseln und Mikrokapseln,
8) Biologie, zur Immobilisierung von Enzymen,
9) Emulgatoren für Glasuren, Polituren, Antischaummittel, milchartige Flüssigkeiten und Stabilisatoren in der Keramik- und Waschmittelindustrie.

22. Sanitäre und chirurgische Artikel, enthaltend einen Ester eines sauren Polysaccharids, ausgewählt aus Carboxymethylcellulose, Carboxymethylstärke und Carboxymethylchitin, mit Alkoholen der aliphatischen, araliphatischen, cycloaliphatischen und heterocyclischen Reihe nach Anspruch 1.

23. Sanitäre und chirurgische Artikel nach Anspruch 22, umfassend einen vollständigen Ester eines sauren Polysaccharids nach einem der Ansprüche 1 bis 13.

24. Sanitäre und chirurgische Artikel nach Anspruch 22 oder 23 in Form eines Filmes.

25. Sanitäre und chirurgische Artikel nach Anspruch 22 oder 23 in Form eines Fadens.

26. Sanitäre und chirurgische Artikel nach Anspruch 22 oder 23 in Form eines Fadens für Wundnähte für chirurgische Operationen.

27. Sanitäre und chirurgische Artikel nach Anspruch 22 oder 23 in Form von Filmen zur Verwendung als künstliche Haut in der Dermatologie.

28. Sanitäre und chirurgische Artikel nach Anspruch 22 oder 23 in Form von Kapseln zur subkutanen Implantation von Medikamenten.

29. Sanitäre und chirurgische Artikel nach Anspruch 22 oder 23 in Form von Mikrokapseln für eine subkutane, intramuskuläre oder intravenöse Injektion.

30. Sanitäre und chirurgische Artikel nach Anspruch 22 oder 23 in Form von festen Einlagen, die nach einer bestimmten Zeitdauer entfernt werden sollen.

31. Sanitäre und chirurgische Artikel nach Anspruch 22 oder 23 in Form eines Schwamms zur medizinischen Behandlung von Verletzungen und Läsionen.

32. Verfahren zur Herstellung eines vollständigen Esters von sauren Polysacchariden nach einem der Ansprüche 1 bis 13, umfassend die Behandlung eines quartären Ammoniumsalzes eines Polysaccharids mit einem etherbildenden Mittel in einem aprotischen Lösungsmittel bei einer Temperatur zwischen 0 und 100 °C.

33. Verfahren nach Anspruch 32, wobei das Lösungsmittel Dimethylsulfoxid ist.

34. Verfahren nach Anspruch 32, wobei das quartäre Ammoniumsalz ein niederes Tetraalkylammoniumsalz ist.

35. Verfahren zur Herstellung eines Arzneimittels nach einem der Ansprüche 14 bis 18, umfassend die Kombination des Wirkstoffes mit einem pharmazeutisch verträglichen Vehikel.

Revendications

1. Esters totaux de polysaccharides acides choisis dans le groupe formé de carboxyméthylcellulose, carboxyméthylamidon et carboxyméthylchitine, dans lesquels les groupes carboxy desdits polysaccharides sont estérifiés par un alcool des séries aliphatique, araliphatique, cycloaliphatique et hétérocyclique, les alcool des séries aliphatiques comportant au maximum 34 atomes de carbone et sont non substitués ou substitués par un ou deux groupes fonctionnels choisis dans le groupe formé par les groupes amino, hydroxy, mercapto, aldéhydo, kéto, carboxy, hydrocarbyle et dihydrocarbylamino, éther, ester, thioéther, thioester, acétal, kétal, carbalkoxy, carbamique et carbamique substitués par un ou deux groupes alkyle, les radicaux hydrocarbyles dans ces groupes modifiés de façon fonctionnelle comportant un maximum de six atomes de carbone, et dans lesquels ces alcools de la série aliphatique peuvent être interrompus dans la chaîne carbonée par des hétéroatomes choisis dans le groupe formé par oxygène, soufre et azote,

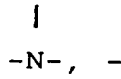
les alcools de la série araliphatique sont ceux comportant un seul résidu benzène et dans lesquels la chaîne aliphatique comporte au maximum quatre atomes de carbone et dans lesquels le résidu benzène peut être substitué par un à trois groupes méthyle ou hydroxy, par des atomes d'halogène, et dans lesquels la chaîne aliphatique peut être substi-

tuée par une ou deux fonctions choisies dans le groupe formé par,

groupes mono-ou diéthyle ou amino libre ou par des groupes pyrrolidine ou pipéridine, et

les alcools des séries cycloaliphatique ou aliphatique-cycloaliphatique ou hétérocyclique proviennent respectivement d'hydrocarbures mono- ou polycycliques comportant au maximum trente quatre atomes de carbone et sont non substitués ou substitués par un ou plusieurs groupes fonctionnels choisis dans le groupe formé par amino, hydroxy, mercapto, aldéhydo, kéto, carboxy, hydrocarbyle et dihydrocarbyle amino, éther, ester, thioéther, thioester, acétal, kétal, carbalkoxy, groupes carbamique et carbamique substitués par un ou deux groupes alkyles, les radicaux hydrocarbyles dans ces groupes modifiés du point de vue fonctionnel comportant au maximum six atomes de carbone, et peuvent être interrompus dans la chaîne carbonée par des hétéroatomes

choisis dans le groupe formé par -O-,



-S-, et peuvent comporter une ou plusieurs liaisons, incluant des structures aromatiques.

2. Esters de polysaccharides acides selon la revendication 1, dans lesquels ledit alcool de la série aliphatique comporte au maximum douze atomes de carbone, lesdits radicaux hydrocarbyles comportent au maximum 4 atomes de carbone et dans lesquels lesdits groupes amino ou carbamiques substitués peuvent également être des groupes alkylènamino ou alkylènecarbamique comportant au maximum 8 atomes de carbone.

3. Esters de polysaccharides acides selon la revendication 2, dans lesquels ledit alcool correspond à alcool éthylique, propylique, isopropylique, n-butylique, isobutylique, tertbutylique, amylique, pentylique, hexylique ou octylique.

4. Esters de polysaccharides acides selon la revendication 2, dans lesquels ledit alcool est de la glycérine.

5. Esters de polysaccharides acides selon la revendication 2, dans lesquels ledit alcool estérifiant est de l'alcool tartronique, acides lactiques, acides glycolique, malique, un acide tartrique ou citrique.

6. Esters de polysaccharides acides selon la revendication 2, dans lesquels l'alcool estérifiant est aminoéthanol, aminopropanol, n-aminobutanol ou les dérivés amino diméthyle ou amino diéthyle en dérivant, choline, pyrrolidinyléthanol, pipéridinyléthanol, pipérazinyléthanol ou les dérivés n-propyle ou n-butyle alcool correspondants, ou monothioéthylèneglycol ou ses dérivés alkyle mercapto inférieurs.

7. Esters de polysaccharides acides selon la revendication 2, dans lesquels le composant alcool estérifiant est un alcool aliphatique supérieur choisi dans le groupe formé par alcool cétylique et myricylique, citronellol, géraniol, nérol, nérolidol, linalool, farnesol et phytol.

8. Esters de polysaccharides acides selon la revendication 1 dans lesquels l'alcool araliphatique est choisi dans le groupe formé par alcool benzylique, phénéthylique, éphédrine et adrénaline.

9. Esters de polysaccharides acides selon la revendication 1 dans lesquels les alcools cycliques sont des alcools monocycliques comportant au maximum 12 atomes de carbone et le cycle comportant entre 5 et 7 atomes de carbones éventuellement substitué par un à trois groupes alkyles inférieurs.

10. Esters de polysaccharides acides selon la revendication 1, dans lesquels les alcools polycycliques sont stérines, acides choliques ou alcools stéroïdiques.

11. Esters de polysaccharides acides selon la revendication 1, dans lesquels les alcools sont choisis dans le groupe formé par alcaloïdes, phénéthylamines, médicaments à base de phénothiazine, thioxanthènes et sulfamides.

12. Un ester d'un polysaccharide acide selon la revendication 1, dans lequel ledit ester est un composé choisi dans le groupe formé par un éthyle, isopropyle, benzyle, p-bromo-benzyle et mirystyle ester de carboxyméthylchitine.

13. Un ester d'un polysaccharide acide selon la revendication 1, dans lequel ledit ester est un composé choisi dans le groupe formé par un éthyle, isopropyle, benzyle, p-bromo-benzyle et mirystyle ester de carboxyméthylcellulose.

14. Une préparation pharmaceutique comprenant en tant que principe actif un ester selon l'une quelconque des revendications 1 à 12.

15. Une préparation pharmaceutique selon la revendication 14 pour une administration par voie parentérale.

16. Une préparation pharmaceutique ou médicament qui comprend:
1) une substance pharmacologiquement active ou une association de substances pharmacologiquement actives; et
2) un véhicule comprenant un ester total selon les revendications 1-13.

17. Une préparation pharmaceutique ou médicament qui comprend un ester total selon les revendications 1-13 dans lesquelles au moins l'un desdits alcools est actif du point de vue thérapeutique.

18. Une préparation pharmaceutique ou médicament selon l'une quelconque des revendications 16 et 17 dans lequel le principe actif est destiné à une utilisation topique.

19. Utilisation thérapeutique d'esters totaux de polysaccharides acides choisis dans le groupe formé par carboxyméthylcellulose, carboxyméthylamidon et carboxyméthylchitine avec des alcools des séries aliphatique, araliphatique, cycloaliphatique et hétérocyclique selon la revendication 1.

20. Utilisation d'un ester d'un polysaccharide acide choisi dans le groupe formé par carboxyméthylcellulose, carboxyméthylamidon et carboxyméthylchitine avec les alcools des séries aliphatique, araliphatique, cycloaliphatique et hétérocyclique selon la revendication 1 dans le domaine cosmétique.

21. Utilisation d'un ester d'un polysaccharide acide choisi dans le groupe formé par carboxyméthylcellulose, carboxyméthylamidon et carboxyméthylchitine avec les alcools des séries aliphatique, araliphatique, cycloaliphatique et hétérocyclique selon la revendication 1 dans l'un des domaines suivants:
1) industrie alimentaire
2) industrie du papier
3) produits adhésifs
4) imprimerie
5) teinture des textiles
6) préparation d'articles sanitaires, médicaux et chirurgicaux
7) galéniques, pour la préparation de gélules et micro-gélules
8) biologie, pour l'immobilisation d'enzymes
9) émulsifiants pour émaux, vernis, agents antimousse, acides lactiques et agents stabilisants, dans l'industrie des céramiques et des détergents.

22. Articles sanitaires et chirurgicaux contenant un ester d'un polysaccharide acide choisi dans le groupe formé par carboxyméthylcellulose, carboxyméthylamidon et carboxyméthylchitine avec les alcools des séries aliphatique, araliphatique, cycloaliphatique et hétérocyclique selon la revendication 1.

23. Articles sanitaires et chirurgicaux selon la revendication 22 qui comprennent un ester total d'un polysaccharide acide selon l'une quelconque des revendications 1-13.

24. Articles sanitaires et chirurgicaux selon l'une des revendications 22-23 sous la forme d'un film.

25. Articles sanitaires et chirurgicaux selon l'une des revendications 22-23 sous la forme d'un fil.

26. Articles sanitaires et chirurgicaux selon l'une des revendications 22-23 sous la forme de fils de suture pour les opérations chirurgicales.

27. Articles sanitaires et chirurgicaux selon l'une des revendications 22-23, sous la forme de films pour une utilisation en tant que peau artificielle en dermatologie.

28. Articles sanitaires et chirurgicaux selon l'une des revendications 22-23, sous la forme de gélules pour un implant sous cutané de médicaments.

29. Articles sanitaires et chirurgicaux selon l'une des revendications 22-23, sous la forme de micro-gélules pour une injection sous cutanée intramusculaire ou intraveineuse.

30. Articles sanitaires et chirurgicaux selon l'une des revendications 22-23 sous la forme d'inserts solides pouvant être retirés après une certaine période de temps.

31. Articles sanitaires et chirurgicaux selon l'une des revendications 22-23 sous la forme d'éponges pour la médication des blessures et des lésions.

32. Un procédé de préparation d'un ester total de polysaccharide acide selon les revendications 1 à 13 qui comprend le traitement d'un sel d'ammonium quaternaire d'un polysaccharide avec un agent éthérifiant dans un solvant apro-

tique à une température de 0 à 100 °C.

33. Un procédé selon la revendication 32, dans lequel ledit solvant est du diméthylsulfoxyde.

34. Un procédé selon la revendication 32, dans lequel ledit sel d'ammonium quaternaire est un sel de tétraalkylammonium inférieur.

35. Un procédé de préparation d'une préparation pharmaceutique selon les revendications 14 à 18, qui comprend la combinaison du principe actif avec un véhicule pharmaceutiquement acceptable.